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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,663	01/29/2004	Yossi Gross	SC&C-100US	5982

23122 7590 07/10/2008

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EXAMINER	
MAEWALL, SNIGDHA	
ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
07/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/767,663	GROSS ET AL.	
	Examiner	Art Unit	
	Snigdha Maewall	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,10-22,26,27,36,41-44,48-59,61-70 and 79-130* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10-22,26,27,36,41-44,48-59,61-70 and 79-130* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/29/07, 12/28/07 and 03/28/08 and 07/02/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

1. Receipt of IDS filed on 11/29/07, 12/28/07, 03/28/08 and 07/02/08 is acknowledged.

The double patenting rejections made in office action dated 10/18/07 have been withdrawn in view of the filing of terminal disclaimers.

The rejections made under 35 USC 112.2 and 112.1 have been withdrawn in view of applicants amendments to the claims.

Claims 1, 3-7, 13-15, 18-19, 21, 26-27, 36, 41-44, 48, 51-53, 55-59, 61-63, 67, 70, 79-81, 87, 94-95, 97-99, 102-104, 108-109, 111, 113, 119-120, 122, and 127-130 have been currently amended.

Claims 131-173 remain withdrawn.

Claims 8-9, 23-25, 28-35, 37-40, 45-47, 60, 71-78, have been cancelled.
Accordingly claims **1-7, 10-22, 26-27, 36, 41-44, 48-59, 61-70 and 79-130** are under prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-7, 10-22, 26-27, 36, 41-44, 48-57, 59, 61-70, 79-87 and 89-130 are rejected under 35 U.S.C. 103(a) as being unpatentable over GB 2374149 A Patent to (Thomas et al.) in view of the combination of references of (Kobonez et al. US Patent No. 6,453,199 B1, Gross et al. US Patent No. 5,925,030 and Yona et al. WO02/098501).

Thomas et al. teaches a swallowable intrabody drug-dispensing capsule comprising a capsule with a sensing module (chemical or electrical), a bio active substance dispenser. The sensing module detects one or more biological conditions within a body. The picture on the front page depicts an embodiment showing drug release into the human digestive system (abstract). Thomas et al. also disclose a method of drug delivery using the medical device. Thomas et al. further disclose that ingestible medical capsules are known which are capable of sensing a condition such as pH, temperature within the digestive tract and then transmitting that sensed data to receiver to help identify a body location for dispensing a drug (page 3, lines 1-5). The transmitter and receiver are disclosed as wireless communication aids which help in initiating drug delivery (see page 8, lines 10-30). A suitable power supply includes lithium battery

which is non toxic to the body (page 10, lines 10-20). Sensing module can be selected to sense absolute values of pH and also could sense presence of unexpected digestive tract constituent such as blood or cancer cells (see page 17, lines 17-25).

Thomas does not teach control component comprising electrodes, control units etc.

Kobozev teaches an invention which relates to medical technology and comprises electrical gastro-intestinal tract and mucous membrane stimulators. The gastrointestinal stimulator comprises electrodes, a device for receiving signals from internal organs and /or external transmitter. The stimulator can comprise additional electrodes. The dimensions of the stimulator can be such that it can be used orally, rectally or vaginally (abstract). The control unit, pulse generator, receiver transmitter are depicted in figure 4. The control unit can also send pulse series to the electrodes and change pulse parameters (current, voltage, duration, frequency etc.). Kobozev further suggests that the electrode be made from non-toxic biologically neutral materials (see the detailed description on column 7, lines 30-55).

Kobozev does not teach self expansible portion, however, Gross et al. teaches self expansible portion in a capsule.

Gross et al. teaches oral drug delivery device having a housing with walls of water permeable material and having at least two chambers separated by a displaceable membrane. The first chamber receives drug and has orifice through which the drug is dispensed under pressure. The second chamber includes electrode forming a part of electrical circuit, which is closed by the ingress of an aqueous ionic solution

into the second chamber. When the current flows through the circuit, gas is generated and acts on the displaceable membrane to compress the first chamber and expel the active ingredient through the orifice (abstract). Gross et al. further discloses that the electric circuit can include sensors such as pH sensor, to effect delivery of the drug to the predetermined region of the gastrointestinal tract, a temperature sensor, sound sensor. Such biosensors can provide feedback to the electric circuit (see column 3, lines 20-30). Various active ingredients can be solid, liquid or semi solid (column 5, lines 62-65).

Yona et al. also discloses a method of treating tumor tissue of an individual. The apparatus requires electrode system. The electrode system is in communication with power source and provides AC input and DC output (see page 23 ,lines 25-30). Various frequencies and electric field pulses are disclosed on page 24, lines 5-25). The apparatus includes an injector mechanism which serves for injecting a cytotoxic agent. (see page 25, lines 5-20 and claims).

Based on the teachings of the above cited references, it would have been obvious to the one of ordinary skilled in the art at the time the invention was made to include driving mechanism comprising control unit pulse generator and multiple electrodes as forwarded by Kobozev et al. and Yona et al. in the teachings of Thomas et al. and Gross et al. which teaches environmentally sensitive mechanism comprising pH sensor and self expansible system taught by Gross et al. with an expectation of obtaining a driving mechanism which is adapted to drive current through the electrode. A skilled artisan would have been motivated to formulate an ingestible capsule

comprising drug , an environmentally sensitive mechanism adapted to undergo the change of state when the capsule is in various stages of gastrointestinal tract with a reasonable expectation of success.

Response to Arguments

4. Applicant's arguments filed 03/28/08 have been fully considered but they are not persuasive.

Applicant argues that the "stimulator in Kobozev's reference is intended to be therapeutic in and of itself, and the patent as a whole lacks any significant reference to administration of drugs. The control unit of the Kobozev stimulator is not adapted to form openings in tight junctions of the epithelial layer of a subject's gastrointestinal tract." Applicants arguments are not persuasive since the reference teaches the control components which are same as the claimed invention, therefore the function of adapting to form openings in tight junction of epithelial layer of a subjects gastrointestinal tract is associated with the components. Additionally, the reference teaches mucous membrane stimulators, one skilled in the art would expect the control components to stimulate mucous membranes which are also part of gastrointestinal tract. It should be noted that the rejection is not anticipation rather an obviousness rejection.

Applicants have indicated in their arguments that the instant specification states:

[0353] In accordance with some embodiments of the present invention, the electrotransport may include any one of, or a combination of, iontophoresis, electroosmosis, and electrophoresis, which enhance diffusion processes through the epithelial cells, and, for some applications, additionally electroporation, which physically punctures or **opens**

biological barriers, along the tight junctions of the epithelial cell boundaries, enabling passage of large molecules through the epithelium."

It is therefore obvious that the combination of electrodes and electron transport system would result in the claimed invention of enabling passage of large molecules through the epithelium. Based on the teachings of the above cited references, it would have been obvious to the one of ordinary skilled in the art at the time the invention was made to include driving mechanism comprising control unit pulse generator and multiple electrodes as forwarded by Kobozev et al. and Yona et al. in the teachings of Thomas et al. and Gross et al. which teaches environmentally sensitive mechanism comprising pH sensor and self expansible system taught by Gross et al. with an expectation of obtaining a driving mechanism which is adapted to drive current through the electrode. A skilled artisan would have been motivated to formulate an ingestible capsule comprising drug , an environmentally sensitive mechanism adapted to undergo the change of state when the capsule is in various stages of gastrointestinal tract with a reasonable expectation of success.

5. Claims 58 and 88 are rejected under 35 U.S.C. 103(a) as being unpatentable over GB 2374149 A Patent to (Thomas et al.) in view of the combination of references of (Kobonez et al. US Patent No. 6,453,199 B1, Gross et al. US Patent No. 5,925,030 and Yona et al. WO02/098501) and further in view of Leonard et al. (Pharmaceutical research vol. 17, no. 4, 2000).

The references taught above do not disclose iontophoretic current between the first and the second electrode. However, Leonard et al. has shown the iontophoresis-enhanced absorptive flux of polar molecules across intestinal tissue in vivo. Leonard et al. further disclose that the eletrophoretic manipulations can modify intestinal absorption of drugs that have otherwise low bioavailability after oral administration (see last paragraph on page 478).

It would have been obvious to the one of ordinary skilled in the art at the time the invention was made to introduce iontophoretic current between the electrodes in order to obtain better absorption of the drugs with a reasonable expectation of success.

Response to Arguments

6. Applicant's arguments filed 03/28/08 have been fully considered but they are not persuasive.

Applicant argues that

" the Leonard article describes the use of iontophoresis to increase drug passage through the epithelial lining of the gastrointestinal tract. Iontophoresis is not the invention recited in currently amended claims 1, 129, and 130. The apparatus of the currently amended independent claims increases absorption by forming openings in the tight junctions of the epithelial layer. Iontophoresisisa method for pushing a drug through a surface, and is clearly distinguished, in the specification of the current application, from the invention as recited in the independent claims of the present patent application."

Applicants arguments are not persuasive because claims 58 and 88 as currently recited have limitations of iontophoretic current. Prior art as cited above, shows the iontophoresis- enhanced absorptive flux of polar molecules across intestinal tissue in vivo. Leonard et al. further disclose that the eletrophoretic manipulations can modify

intestinal absorption of drugs that have otherwise low bioavailability after oral administration (see last paragraph on page 478).

It would have been obvious to the one of ordinary skilled in the art at the time the invention was made to introduce iontophoretic current between the electrodes in order to obtain better absorption of the drugs with a reasonable expectation of success.

The rejection is therefore maintained.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-0580.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business

Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Snigdha Maewall/
Examiner, Art Unit 1612

/Gollamudi S Kishore, Ph.D/
Primary Examiner, Art Unit 1612